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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/782,435	02/18/2004	Pramod B. Mahajan	1121C	6412

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PIONEER HI-BRED INTERNATIONAL INC.
7100 N.W. 62ND AVENUE
P.O. BOX 1000
JOHNSTON, IA 50131

EXAMINER	
IBRAHIM, MEDINA AHMED	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/782,435	MAHAJAN, PRAMOD B.	
	Examiner	Art Unit	
	Medina A. Ibrahim	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

HL

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's response filed 01/25/05 in reply to the Office action of 08/25/04 has been entered. Claims 5 and 15 have been amended. Claims 1-27 are pending and are examined. It is noted that the serial number of the instant application on pages 3-16 of the response is incorrect.

All previous objections and rejections not set forth below have been withdrawn. This Office action contains NEW GROUNDS OF REJECTIONS not necessitated by Applicant's amendments. Therefore, this action is non-final. The delay in applying these grounds of rejection is regretted.

Claim Rejections - 35 USC § 112

Claims 1-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to an isolated polynucleotide comprising the nucleic acid sequence of SEQ ID NO: 3 encoding SEQ ID NO: 4, a recombinant expression cassette, a host cell and transgenic plant/cell comprising said nucleic acid sequence, and a method for modulating the level of RuvB in a plant/plant cell with said nucleic acid sequence. The claims are also drawn to polynucleotide sequences having at least 80%,

85%, and 90% sequence identity to SEQ ID NO: 3 and encoding a polypeptide having RuvB activity, or nucleic acid sequences encoding polypeptides having at least 80%, 85%, and 90% sequence identity to SEQ ID NO: 4 and having RuvB activity.

The specification states that SEQ ID NO: 3 from maize encodes a polypeptide having RuvB activity involved in homologous recombination. On the paragraph bridging pages 2 and 3 of the specification, Applicant states "RuvB has two NTP binding motifs, known as Walker A and Walker B boxes, as well as other structural motifs common to DNA helicases ..... However, the functional form of this enzyme is thought to be a hexamer. Two hexameric RuvB units bind to DNA in a symmetrical manner to form a ring, similar to the hexameric..... However, a RuvAB complex functions much more robustly, and requires less Mg+2. Thus, RuvB participates in one of the rate limiting steps in homologous recombination in all living organisms". The specification also states that expression of said polynucleotide in a transgenic plant provides the means to modulate the efficiency with which nucleic acids of interest are incorporated into the genomes of a target plant cell.

The specification, however, fails to teach how to use the isolated polynucleotide of SEQ ID NO: 3 to provide an agronomic trait in a transgenic plant. Neither the instant specification nor the prior art provides the biological function of a RuvB polynucleotide/polypeptide in a plant or its specific role in DNA repair process or homologous recombination. According to Applicant's response on page 12 (line 7), no plant RuvB homologue has been identified/isolated before Applicant's invention. The instant specification provides no working examples as to specific biological function of

the claimed polynucleotide, and one of ordinary skill in the art would not be able to predict what activity would be possessed by the RuvB polynucleotide or polypeptide based solely because it has the two NTP binding motifs, known as Walker A and Walker B boxes, as well as other structural motifs common to DNA repair polynucleotide or polypeptide. Applicant has not provided test data, affidavits and/or declaration, or a printed publication to support the role of RuvB in plant DNA repair process or in integration of a desired DNA into a plant genome.

DNA repair and synthesis are complex processes involving numerous interacting proteins and enzymes, many of which have yet to be identified in plants as evidenced by Applicant's own disclosure. The prior art provides limited information regarding the specific biological activity of a RuvB polypeptide. Furthermore, using the instant polynucleotide to modulate the level of RuvB in the plant is not a specific biological activity, because a polynucleotide need not encode a RuvB polypeptide in order to modulate level of RuvB in a plant. Therefore, without knowing the biological activity for the claimed polynucleotide encoding a RuvB polypeptide, one of ordinary skill in the art would not be able to use it or predict a phenotypic effect for it, simply because it comprise two NTP binding motifs, known as Walker A and Walker B boxes, as well as other structural motifs common to DNA repair proteins. Therefore it is impossible to predict the phenotypic effect of SEQ ID NO: 3 upon expression in a transgenic plant. Furthermore, it is unclear how a modulate level of the RuvB protein would affect the DNA repair process or integration of desired polynucleotide into the plant genome, since other proteins such as RuvA are also involved.

Therefore, given the lack of guidance in the specification regarding how to use the claimed polynucleotide; the limited information on polypeptides with RuvB activity and their specific biological function; lack of working examples in the specification; and the unpredictability inherent in predicting the biological activity of a protein based on specific conserved regions; and the nature of the invention as discussed above, one skilled in the art would not know how to use the claimed SEQ ID NO: 3 without undue trial and error experimentation. Consequently, one would not know how to use polynucleotide sequences having at least 80%, 85%, and 90% sequence identity to SEQ ID NO: 3 and polynucleotide sequences encoding polypeptides having at least 80%, 85%, and 90% sequence identity to SEQ ID NO: 4; since no specific biological function has been disclosed for SEQ ID NO: 3 encoding SEQ ID NO: 4.

In *Genentech Inc. v. Novo Nordisk* A/S (42 USPQ2d 1001 at p. 1005) The CAFC stated "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not workable...While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention...[W]hen there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required...." Like in Genentech, the instant specification does not provide sufficient guidance that enables one skilled in the art to practice the claimed invention without undue experimentation.

In the event that Applicant is able to overcome the above rejection, the scope of

enablement will still be limited to SEQ ID NO: 3 encoding SEQ ID NO: 4, recombinant expression cassette comprising SEQ ID NO: 3 and transgenic plant/host cell transformed with said expression cassette, and a method of transforming a plant with SEQ ID NO: 3, for the reasons discussed in the last Office action of 08/24/05.

Response to Arguments

Applicant correctly states that the test for enablement is whether one skilled in the art could make or use the invention based on the teachings of the disclosure coupled with the prior art information. Applicant asserts that the disclosed full-length polynucleotides from corn and the identified conserved domains as well as the teaching of the prior art regarding other RuvB homologues and assays for testing RuvB activity are sufficient to enable one skilled in the art to practice the full scope of the claims. Applicant cites Qui et al (J. Biol. Chem. 273(43): 27786-27798); Makino et al (Biochem. Biophys. Res. Comm. 245:819-823 (1998); Kishimoto et al (EP 0926 157 A1); and Kurokawa et al to support this position (response, p. 13).

These are not persuasive because the specification doesn't teach which region in the full-length sequence is sufficient to encode a functional polypeptide having the desired biological function. The 35 USC 112, 1st and supporting case law do not require that Applicant exemplifies all nucleic acid or polypeptide sequences having at least 80%, 85%, and 90% sequence identity to SEQ ID NO: 3 or 4 and having RuvB activity. However, as agreed by Applicant, the disclosure must contain sufficient guidance to enable a person skilled in the art to carry out the invention commensurate with scope of the claims. That has not been done in the instant specification.

The specification discloses unmodified sequences and merely provides general guidance on methods for altering single amino acid or conservative amino acid substitutions in given nucleotide/protein sequence to produce variants. For example, on pages 7 and 8 of the specification discusses about conservatively modified nucleic acid variants or silent variants that encode identical or conservatively modified variants of the amino acid sequences. However, according to Lazar et al disclosed in last Office action, conserved amino acid substitutions does not necessarily provide predictable results. Lazar showed that the conservative substitution of glutamic acid for aspartic acid at position 47 changed the biological function of transforming growth factor-alpha, while non-conservative substitutions with alanine or aspargine had no effect. Therefore, without specific guidance as to which modifications would allow SEQ ID NO: 3 retain both the structural and functional limitations as recited in the claims, one cannot predict whether any and all with nucleic acid or polypeptide sequences having at least 80%, 85%, and 90% sequence identity to SEQ ID NO: 3 or 4 would retain RuvB activity.

While determination of sequence identity and assays of testing protein activity are well within the level of one skilled in the art, specific guidance are required to modify SEQ ID NO: 3 so that a nucleic acid sequences having both the desired structural and functional characteristics can be obtained. One skilled in the art would have to make all possible nucleotide substitutions and deletions in SEQ ID NO: 3, and test all nucleotide sequences that meet the structural limitation to determine which also meet the functional limitation. One would also have to evaluate the ability of the claimed variants

to affect DNA repair protein or integration of a desired DNA into a plant genome. These tests are considered undue.

Regarding the references cited by Applicant, it is noted that none of the cited reference establishes a specific biological function for a RuvB homologue or teach expression of a RuvB in a transgenic plant. For example, Qui et al (J. Biol. Chem. 273(43): 27786-2779891998)) teach isolated and purified human RuvB (RuvBL1) having sequence similarity with the bacterial RuvB protein. However, RuvBL1 failed to show any ATPase activity, even at high ATP concentration, when expressed in the insect baculovirus system (see Results on page 27788, and Fig. 4A). These results further support the previously cited reference's teaching that sequence homology is not predictive of function (see Lazar et al, cited in the last Office action). Given this unpredictability, it is impossible to predict the phenotypic effect of SEQ ID NO: 3 when expressed in a transgenic plant. Trial and error experimentation would be required.

With respect to *John Hopkins v. Cellpro* cited in the response, it is noted that the instant specification does not enable even one mode of making the claimed invention. Therefore, the case law does not appear to support Applicant's position.

Therefore, in view of the reasons discussed above and in the last Office action, the claimed invention is not enabled throughout the broad scope.

Written Description

Claims 1-27 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. This rejection is repeated for the reasons of record as set forth in the Office action mailed 08/25/04. Applicant's arguments filed 01/25/05 have been fully considered but are not deemed persuasive.

Applicant argues that the instant specification describes four full-length nucleic acid sequences from maize and further describes other homologues having percent sequence identity, and further demonstrates conserved RuvB domains. Applicant further argues that Makino et al describes Elisa and immunology assays, while Kishimoto et al further discloses ATPase and helicase assays. Applicant further cites Kurokawa et al who teach sequence conservation of TIP49 homologues among organisms (response, p. 14-15).

Applicant's arguments are not persuasive because the specification does not describe a representative number of polynucleotides of the genus claimed. While the instant specification describes four full-length nucleic acid sequences, they are all from a single plant species, corn. Neither the prior art nor the instant specification describes the specific biological function of a plant RuvB homologue. The prior art teachings of Elisa, immunoassays, and ATPase/ helicase assays do not support the written description requirement. The disclosed conserved domains are not unique to RuvB but are common to all DNA repair proteins, and do not constitute a substantial portion of the genus of the claims. Therefore, the disclosed sequences are not representative species of the claimed genus. Therefore, in view of the above and in the last Office action, the claimed invention is not adequately described.

Double Patenting

Claims 1-27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6, 706, 949. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in both the application and patent are directed to the nucleic acid sequence of SEQ ID NO: 3 or sequences having % identity thereof, a recombinant expression cassettes, host cells, and transgenic plant comprising said nucleic acid sequence, and a method for modulating the level of RuvB in a plant. This rejection is repeated for the reasons of record as set forth in the Office action mailed 08/25/04. Applicant has not addressed this rejection. Therefore, the rejection is maintained.

Remarks

The claims are deemed free of the prior art because the prior art does not teach or reasonably suggest a nucleic acid sequence having at least 80%, 85%, or 90% sequenc identity to SEQ ID NO: 3. Nor that the prior art teaches, a recombinant expression cassette transgenic plant comprising said nucleic acid sequences, or a method that employs said nucleic acid sequence.

No claim is allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is (571) 272-0797. The Examiner can normally be reached Monday -Thursday from 8:00AM to 5:30PM and every other Friday from 9:00AM to 5:00 PM. Before and after final responses should be directed to fax nos. (703) 872-9306 and (703) 872-9307, respectively.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (571) 272-0804.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

4/1/05

Medina A. Ibrahim

MEDINA A. IBRAHIM
PATENT EXAMINER